JC10 Rec'd PCT/PTO 25 JAN 2002

Customized FORM PTO-1390 U.S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTORNEY DOCKET NO P07504US00/BAS
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		10/031950
INTERNATIONAL APPLICATION NO. PCT/GB00/02881	INTERNATIONAL FILING DATE 26 JULY 2000	PRIORITY DATE CLAIMED 27 JULY 1999

TITLE OF INVENTION: HYDROGEN BONDED COMPOUNDS

APPLICANT(S) FOR DO/EO/US: GREENER, Bryan

Applicant herewith submits to the US Designated/Elected Office (DO/EO/US) the following items and other information:

- ☒ 1. This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
- ☐ 2. This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 USC 371.
- ☒ 3. This express request to begin national examination procedures (35 USC 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 USC 371(b) and PCT Art. 22 and 39(1).
- ☒ 4. A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
- ☒ 5. A **copy** of the International Application as filed (35 U.S.C. 371 (c)(2))
  - ☐ a. is transmitted herewith (required only if not transmitted by the International Bureau).
  - ☒ b. has been transmitted by the International Bureau.
  - ☐ c. is not required, as the application was filed in the United States Receiving Office (RO/US).
- ☐ 6. A **translation** of the International Application into English (35 U.S.C. 371(c)(2)).
- ☒ 7. Amendments to the claims of the International Appln. under PCT Article 19 (35 USC 371 (c)(3))
  - ☐ a. are transmitted herewith (required only if not transmitted by the International Bureau).
  - ☐ b. have been transmitted by the International Bureau.
  - ☐ c. have not been made; however, the time limit for making such amendments had NOT expired.
  - ☒ d. have not been made and will not be made.
- ☐ 8. A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
- ☒ 9. An **oath** or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
- ☐ 10. A translation of the annexes to the Int'l Prelim. Exam. Report under PCT Article 36 (35 U.S.C. 371(c)(5))

Items 11. to 20. below concern document(s) or information included:

- ☐ 11. An **Information Disclosure Statement** under 37 C.F.R. 1.97 and 1.98.
- ☒ 12. An **Assignment** document for recording. A separate cover sheet in compliance with 37 CFR 3 28 and 3.31 is included
- ☒ 13. A **First preliminary amendment.**
- ☐ 14. A Second or Subsequent preliminary amendment.
- ☐ 15. A substitute specification.
- ☐ 16. A change of power of attorney and/or address letter.
- ☐ 17. A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 & 35 USC 1 821-825.
- ☐ 18. A second copy of the published international application under 35 USC 154(d)(4).
- ☐ 19. A second copy of the English translation of the international application under 35 USC 154(d)(4).
- ☐ 20. Other items or information:
  - ☐
  - ☐

- ☐ A copy of the Notification of Missing Requirements under 35 U.S.C. 371.
- ☐ In the event that a petition for extension of time is required to be submitted herewith, and in the event that a separate petition does not accompany this response, applicant hereby petitions under 37 CFR 1.136(a) for an extension of time of as many months as are required to render this submission timely. Any fee is authorized in 17(c).

Date: 25 January 2002

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U.S. APPLICATION NO. *(If known)*	INTERNATIONAL APPLICATION NO.	ATTORNEY DOCKET NO.
10/031950	PCT/GB00/02881	P07504US00/BAS

☒ 21. **The following fees are submitted:**

☒ **Basic National Fee** (37 CFR 1.492 (a) (1)-(5):

		CALCULATIONS	*PTO USE ONLY*
☐ Neither Int'l Prelim. Exam. fee nor Int'l Search fee paid to USPTO	$1040		
☒ Search Report has been prepared by the EPO or JPO	$ 890		
☐ No Int'l Prelim. Ex. fee paid to USPTO but Int'l Search fee paid to USPTO	$ 740		
☐ International preliminary examination fee paid to USPTPO	$ 710		
☐ Int'l Prelim. Ex. fee paid to USPTO & all claims satisfied PCT Art. 33(1)-(4)	$ 100		
ENTER APPROPRIATE BASIC FEE AMOUNT =		$ 890	
☐ Surcharge of **$130** for furnishing the oath or declaration later than ☐ 20 mos ☐ 30 mos. from the earliest claimed priority date (37 CFR 1.492(e)).	+	$	

CLAIMS	*NUMBER FILED*	*NUMBER EXTRA*	*RATE*		
Total Claims	15 - 20 =		X **$18** =	$	
Independent Claims	02 - 03 =		X **$84** =	$	
☐ Multiple Dependent Claim(s) (if applicable)			+ **$280** =	$	
TOTAL OF ABOVE CALCULATIONS =				$ 890	
☐ Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by ½.			-	$	
SUBTOTAL =				$ 890	
☐ Processing fee of **$130** for furnishing the **English translation** later than ☐ 20 mos. ☐ 30 mos. from the earliest claimed priority date (37 CFR 1.492(f)).			+	$	
TOTAL NATIONAL FEE =				$ 890	
☒ Fee for recording the enclosed **assignment** (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3 28, 3.31) **$40** per property			+	$ 40	
TOTAL FEES ENCLOSED =				$ 930	
			Amount to be	*Refunded*	$
				Charged	$

☒ a. A **check** in the amount of $930 to cover the above fees is enclosed.

☐ b. Please charge my Deposit Account No. 12-0555 in the amount of $ to cover the above fees.

☒ c. The Commissioner is hereby authorized to charge any additional fees required or credit overpayment to Deposit Account No. 12-0555.

Note: *Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.*

SEND ALL CORRESPONDENCE TO:

B. Aaron Schulman

At the address (below) of **CUSTOMER NO. 00881.**

LARSON & TAYLOR, PLC
1199 NORTH FAIRFAX ST.
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SIGNATURE: Douglas E. Jackson

NAME: Douglas E. Jackson

REG. NO.: 28518

PHONE NO.: 703-739-4900

Date: 25 January 2002

10/031950
JC13 Rec'd PCT/PTC 25 JAN 2002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent

In re patent application of: GREENER

Serial No.: NEW APPLICATION

Filed: On even date herewith

For: HYDROGEN BONDED COMPOUND

Examiner:

Art Unit:

Dckt No.: P07504US00/BAS

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C.

S I R:

Prior to examination, please amend the above-identified application as follows.

IN THE CLAIMS:

A clean version of the amended claims is provided herewith in **Attachment A**. It will be noted that all the claims have been amended relative to the previously provided version as shown by the marked up version thereof in **Attachment B** provided herewith.

REMARKS

By this Amendment, the claims have been rewritten to reduce the multiple dependencies.

Further and favorable action is solicited.

Respectfully submitted,

Date: 1/25/02

By: Douglas E. Jackson
Douglas E. Jackson
Registration No. 28518

LARSON & TAYLOR PLC - 1199 North Fairfax Street, Suite 900 - Alexandria, Virginia 22314 -

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ATTACHMENT A

Clean Replacement/New Claims (entire set of pending claims)

Following herewith is a clean copy of the entire set of pending claims.

Clean Replacement/New Claims

Following herewith is a clean copy of each claim which replaces each previous claim having the same number; and each new claim.

1. (amended) A supramolecular assembly comprising a plurality of hydrogen bonded molecules, each molecule contains regularly spaced, multiple site hydrogen bonding groups and wherein at least a proportion of the molecules are bonded to other molecules at sites other than at terminal locations.

2. (amended) An assembly as claimed in claim 1 wherein the hydrogen bonded molecules are pharmacologically acceptable.

3. (amended) An assembly as claimed in claim 1 wherein the hydrogen bonding sites are separated by hydrophobic moieties.

4. (amended) An assembly as claimed in claim 1 wherein the hydrophobic moiety is derived from an alkyl diacid or functional derivative thereof.

5. (amended) A compound that is capable of being hydrogen bonded to form a supramolecular assembly having the general formula (I):

$$A\text{-}X\text{-}(N\text{-}X)_n\text{-}A \qquad (I)$$

where:

A may be the same or different and is a moiety containing at least one hydrogen bond donor and/or acceptor sites,

N may be the same or different and is a moiety containing at least one hydrogen bond donor and/or acceptor,

X may be the same or different and is a difunctional spacer linkage or unit, and

n is an integer having a value of at lease one.

6. (amended) A compound as claimed in claim 5 wherein the moieties A and N contain hydroxyl or carboxyl groups.

7. (amended) A compound claimed in claim 5 wherein A is an aromatic moiety of the general formula (II):

$$\begin{matrix} HO- \\ HO- \end{matrix}\!\!\left[Ar\right]\!-COOH \qquad (II)$$

Where Ar is an unsubstituted or substituted aromatic nucleus.

8. (amended) A compound as claimed in claim 7 wherein Ar is phenyl or benzyl.

9. (amended) A compound as claimed in claim 7 wherein the compound of Formula (II) is 2,5-dihydroxybenzoic acid or 2,3-dihydroxybenzoic acid.

10. (amended) A compound as claimed in claim 5 wherein N is a moiety containing at least three hydrogen bond acceptance or donation sites.

11. (amended) A compound as claimed in claim 5 wherein X is an alkyl diacid of the general formula:

$$HOOC\text{-}(CH_2)_m\text{-}COOH$$

wherein m is an integer having a value of at least 2, or a functional derivative thereof

12. (amended) A compound as claimed in claim 11 wherein X is derived from dodecanedioic-, decanedioic-, octanedioic- or hexanedioic acids or an acid chloride thereof.

13. (amended) An assembly comprising the aggregation of compounds of the general formula (I) as defined in claim 5.

14. (amended) An artifact manufactured from an assembly as claimed in claim 1.

15. (new) An artifact manufactured from a compound as claimed in claim 5.

ATTACHMENT B

Marked Up Replacement Claims

Following herewith is a marked up copy of each rewritten claim together with all other pending claims.

1. (amended) A supramolecular assembly comprising a plurality of hydrogen bonded molecules, each molecule contains regularly spaced, multiple site hydrogen bonding groups and wherein at least a proportion of the molecules are bonded to other molecules at sites other than at terminal locations.

2. (amended) An assembly as claimed in claim 1 wherein the hydrogen bonded molecules are pharmacologically acceptable.

3. (amended) An assembly as claimed in claim 1 ~~or claim 2~~ wherein the hydrogen bonding sites are separated by hydrophobic moieties.

4. (amended) An assembly as claimed in ~~any one of claims 1 to 3~~ claim 1 wherein the hydrophobic moiety is derived from an alkyl diacid or functional derivative thereof.

5. (amended) A compound that is capable of being hydrogen bonded to form a supramolecular assembly having the general formula (I):

$$A\text{-}X\text{-}(N\text{-}X)_n\text{-}A \qquad (I)$$

where:

A may be the same or different and is a moiety containing at least one hydrogen bond donor and/or acceptor sites,

N may be the same or different and is a moiety containing at least one hydrogen bond donor and/or acceptor,

X may be the same or different and is a difunctional spacer linkage or unit, and

n is an integer having a value of at lease one.

6. (amended) A compound as claimed in claim 5 wherein the moieties A and N~~,~~ contain hydroxyl or carboxyl groups.

7. (amended) A compound claimed in claim 5 ~~or claim 6~~ wherein A is an aromatic moiety of the general formula (II):

$$\begin{matrix} HO- \\ HO- \end{matrix}[Ar]-COOH \qquad (II)$$

Where Ar is an unsubstituted or substituted aromatic nucleus.

8. (amended) A compound as claimed in ~~any of~~ claim~~s~~ 7 wherein Ar is phenyl or benzyl.

9. (amended) A compound as claimed in ~~any of~~ claim~~s~~ ~~5 to 8~~7 wherein the compound of Formula (II) is 2,5-dihydroxybenzoic acid or 2,3-dihydroxybenzoic acid.

10. (amended) A compound as claimed in ~~any of claims 5 to 9~~ claim 5 wherein N is a moiety containing at least three hydrogen bond acceptance or donation sites.

11. (amended) A compound as claimed in ~~any of claims 5 to 10~~ claim 5 wherein X is an alkyl diacid of the general formula:

$$HOOC-(CH_2)_m-COOH$$

wherein m is an integer having a value of at least 2, or a functional derivative thereof

12. (amended) A compound as claimed in claim 11 wherein X is derived from dodecanedioic-, decanedioic-, octanedioic- or hexanedioic acids or an acid chloride thereof.

13. (amended) An assembly comprising the aggregation of compounds of the general formula (I) as defined in claim 5.

14. (amended) An ~~artefact~~artifact manufactured from an assembly as claimed in ~~any one of~~ claims 1~~ to 4 or from a compound as claimed in any one of claims 5 to 13~~.

15. (new) An artifact manufactured from a compound as claimed in claim 5.

HYDROGEN BONDED COMPOUNDS

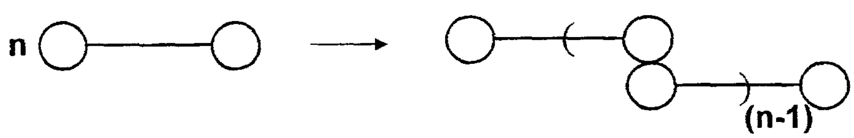
This invention relates to degradable polymer-like materials, in particular to such materials which are biodegradable, to precursors therefor and to artefacts made therefrom such as medical implant devices. More particularly the invention relates to polymer-like materials which can be formed into flexible constructs such as structural blocks, yarns and fibres.

In the conventional understanding of the term polymer, literally, many units, the component sub-units or precursors, eg. monomers or oligomers are bonded together *via* covalent linkages to form a high molecular weight material. Degradation of the polymer into lower molecular weight species occurs by scission of the covalent bonds binding the sub-units or by scission of a bond within one or more of the sub-units. For materials to biodegrade, the scission mechanism is usually a hydrolytic reaction. For a covalently bound polymer artefact to biodegrade completely, the hydrolysis of the polymer may take several years. Thus such polymers may have limited use in environments where constructs made from such polymers are required to have a temporary existence. Even in those cases where hydrolysis of the covalent bond, for example an anhydride linkage, takes place rapidly there has been no ability to control the precise nature of the degradation product. Thus, in some instances it may be desirable to degrade the polymer to lower molecular weight, non-toxic molecules, such as carbon dioxide and water, but in others it may be desired to form degradation products which are, themselves, beneficial, for example, exhibit a pharmaceutical effect.

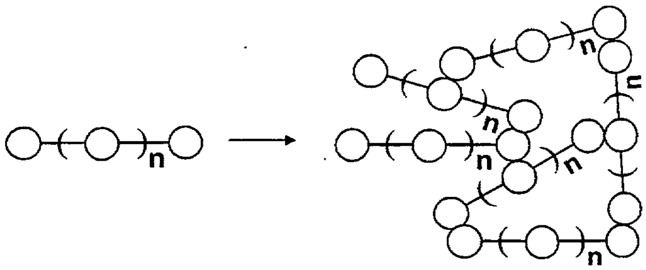
Thus, as an object, the present invention seeks to provide a class of materials which are capable of being formed into artefacts

and yet can be degraded in a predictable and controlled manner to form predictable fragments.

The materials of the present invention are characterised in that although they are polymer-like, the precursor residues are bonded to each other not by covalent bonds but by hydrogen bonds. Previously, this approach has been successfully applied to produce polymeric species by association of molecules with hydrogen bonding groups at their termini (for example, see R. P. Sijbesma, F. H. Beijer, L. Brunsveld, B. J. B. Folmer, J. H. K. K. Hirschberg, R. F. M. Lange, J. K. L. Lowe and E. W. Meijer, *Science*, **1997**, *278*, 1601 and references cited therein):



Such materials have been reported to be linear polymers, with each sub-unit associated to its neighbour at one site (which may be comprised of several hydrogen bonding groups). Because every chain is only as strong as its weakest link, researchers have focused on maximising the number of terminal hydrogen bonding groups. In a departure from this approach, we have produced molecules with multiple, regularly spaced hydrogen bonding sites and, in particular, at non-terminal sites, distinct from the prior art in that intermolecular interactions may occur at many sites and in a networked fashion:



The attachment of molecular components at many interactive sites affords less opportunity for dissociation than those hydrogen bonded molecules or 'assemblies' with only terminal interaction sites reported for prior art species.

In accordance with a first embodiment of the present invention there is provided a supramolecular assembly comprising a plurality of hydrogen bonded molecules, preferably pharmacologically acceptable molecules, each molecule contains multiple site hydrogen bonding groups and wherein at least a proportion of the molecules are bonded to other molecules at sites other than at terminal locations. Aptly the multiple site hydrogen bonding groups are regularly spaced.

In a preferred form of this embodiment the hydrogen bonding sites will be separated by hydrophobic moieties such as a moiety derived from an alkyl diacid

In accordance with a further embodiment of the invention there is provided a compound that is capable of being hydrogen bonded to form a supramolecular assembly and which has the general formula **(I)**:

$$\mathbf{A\text{-}X\text{-}(N\text{-}X)_n\text{-}A} \qquad \mathbf{(I)}$$

where:

A may be the same or different and is a moiety containing at least one hydrogen bond donor and/or acceptor site,

N may be the same or different and is a moiety containing at least one hydrogen bond donor and/or acceptor,

X may be the same or different and is a difunctional spacer linkage or unit

and **n** is an integer having a value of at least one.

In a further embodiment of the invention there is provided a biodegradable composition of matter comprising a super assembly of molecules each having the general formula (I) herein. More preferably, **A** and **N** will contain a plurality of hydrogen bond donor or acceptor sites, typically regularly spaced apart. The **A** moiety will contain at least four hydrogen bond donor or acceptor sites

The moieties **A** and **N**, containing the donor and/or acceptance sites or groups, may be known *per se*. Preferred moieties are those that contain hydroxyl and/or carboxyl groups.

Aptly, **A** is an aromatic moiety. preferably an aromatic moiety of the general formula **(II)**:

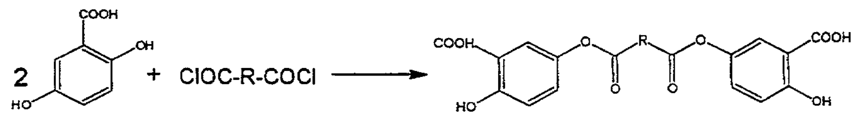
$$\begin{matrix}\mathrm{HO}-\\ \mathrm{HO}-\end{matrix}\!\Big[\ \mathrm{Ar}\ \Big]\!-\mathrm{COOH}$$

(II)

Where **Ar** is an unsubstituted or substituted aromatic nucleus e.g. phenyl or benzyl.

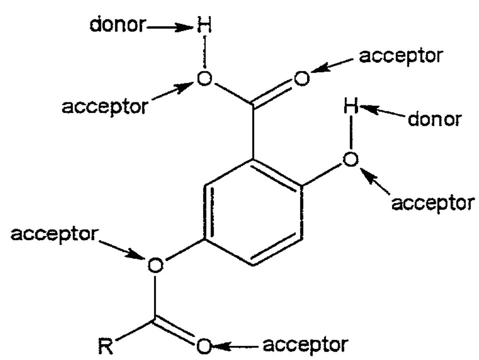
Preferred examples of compounds of Formula II are moieties which are capable of site-specific reactivity with the moiety **X**. Such preferred compounds include 2,5- and 2,3-dihydroxybenzoic acids

For example, when **X** is an alkyl diacid chloride, 2,5 dihydoxybenzoic acid will react according to the equation:



R = $(CH_2)_m$

The disposition of the terminal donor and acceptor sites in this compound may be represented thus:



N is a moiety containing at least one hydrogen bond acceptance or donation site, aptly two or more hydrogen bond donation or acceptance sites, and may preferably contain at least three donors and/or acceptors. Preferably **N** is a moiety which comprises both hydrogen bond donating and accepting sites regularly spaced,

The moiety **N** may be the same or different as the moiety **A**. Aptly, where **A** and **N** are different, **A** may be 2,5-dihydroxybenzoic acid and **N** may be 3,5-dihydroxybenzoic acid.

X is a difunctional linkage or residue and may be any moiety which does not have an adverse effect on the properties of the donor or acceptor groups. Suitably, **X** may comprise one or more

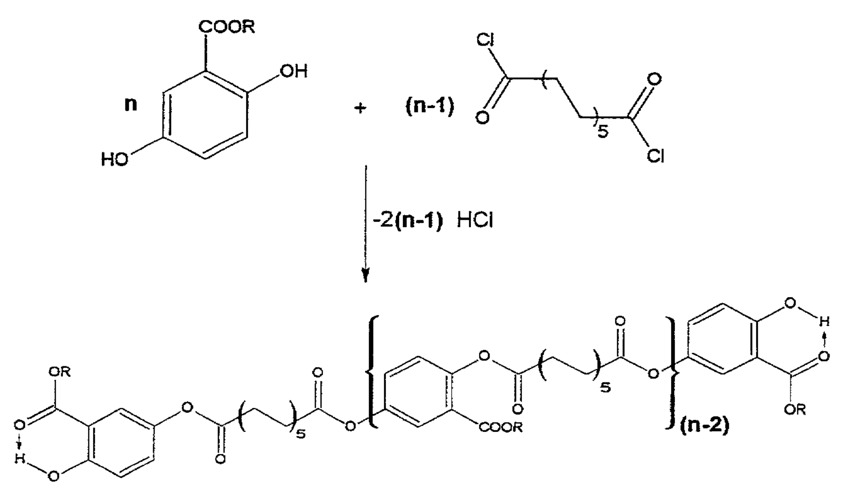
groups which exhibit hydrophobic properties. Aptly, **X** will be a residue which will impart flexibility to aggregates, mixtures or polymers derived from compounds of the invention.

X is preferably comprised, in part or in total, of an alkylene group $(CH_2)_m$ where $m \geq 2$ and more preferably, an alkyl diacid, or a functional derivative thereof, for example of the type,

$$HOOC\text{-}(CH_2)_m\text{-}COOH$$

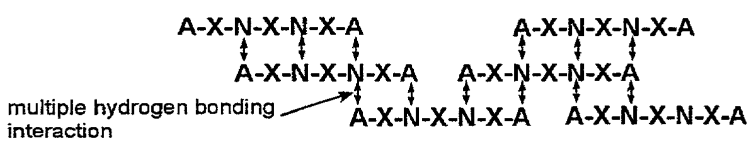
Aptly, the moiety **X** may be derived from long chain acids such as dodecanedioic-, decanedioic-, octanedioic- or hexanedioic acids or functional derivatives thereof such as dodecandioyl dichloride, suberoyl chloride or sebacoyl chloride.

Reactants comprising the precursors of the moieties **A** and **N** and **X** are reacted to form covalent linkages between the species. The methods employed to carry out this reaction may by those conventionally employed. For example, **A** or **N** may be connected to **X** *via* an ester linkage by reacting **A** or **N**, comprising of at least one hydroxyl function, with an acid halide of **X** as shown by the following reaction scheme:



The precursors of the supramolecular assemblies, being compounds and mixtures, as defined above, display aggregative properties in solution and/or in the molten state will henceforth be referred to as 'press-stud oligomers'. Aggregation of press-stud oligomers *via* the interaction of hydrogen bonding sites **A** and **N** allows the formation of supramolecular assemblies (in the form of fibres) when the press stud oligomer mass is melt extruded at elevated temperatures (>50 ^{0}C). Fibres so formed are self adherent and flexible immediately after extrusion. Aggregation can be probed by ^{13}C NMR spectroscopy and viscometric measurements against reference compounds lacking some/all hydrogen bonding functions.

The fibre forming properties of such aggregates, whilst not fully understood, are believed to be related to the abilility of the oligomers to align themselves under extrusion, as shown:



Press-stud oligomers are fibre-forming materials and may be composed of biocompatible and/or therapeutically active compounds (e.g. 2,5-dihydroxybenzoic acid) that are water soluble.

The press-stud oligomers of the present invention may be formed into supramolecular assemblies suitable for use as drug delivery vehicles and adhesives. The press-stud oligomers may be shaped into supramolecular assemblies suitable for medical device applications such as load-bearing fixation plates, screws or tissue anchors. In an alternative use the supramolecular assemblies of the

present invention may have uses outside the medical device field, for example as a biodegradable structural packaging material.

Accordingly, the present invention further provides an artefact formed from the biodegradable compositions of matter as described herein.

The invention will now be further described with reference to the accompanying drawings and the following examples, based on:

2,5-dihydroxybenzoic acid (**G**),
dodecanedioyl dichloride (**D**) and
methyl-2,5-dihydroxybenzoate (**MeG**)

all of which were supplied by Aldrich Chemical Co. Ltd and used as supplied.

In the structural formulae given abbreviations given in upper case text (e.g. $\mathbf{G_3D_4}$) refer to supramolecular assemblies whereas formulae expressed in lower case text (e.g. $\mathbf{g_3d_4}$) refer to the discrete press-stud oligomer form.

IR spectra were collected using a Mattson Galaxy 5020 FTIR spectrometer, samples prepared as cast films from THF for analysis. NMR spectra were collected using a JEOL 270 MHz NMR spectrometer.

Mass spectra were acquired using a Fisons Instruments Autospec Spectrometer. Viscometric measurements were performed using a Carrimed CSL500 constant stress rheometer, using a 4 cm diameter parallel plate and a 200 µm gap. Yields of >85% were recovered from all reactions.

Liquid Chromatography Conditions

Analyses were carried out using a HP 1100 series chromatograph with a Jupiter C18 5µM 150 x 2mm column. Flow rate 0.2ml/min.

HP 1100 DAD 200 to 400nm detector. Samples were dissolved in methanol, injection volume 5 µl. Solvent gradient:

Time / min.	0.1% aqueous trifluoroacetic acid / %vol.	0.1% trifluoroacetic acid in acetonitrile / %vol.
0	50	50
5	50	50
20	10	90
40	10	90

Referring to the accompanying drawings:

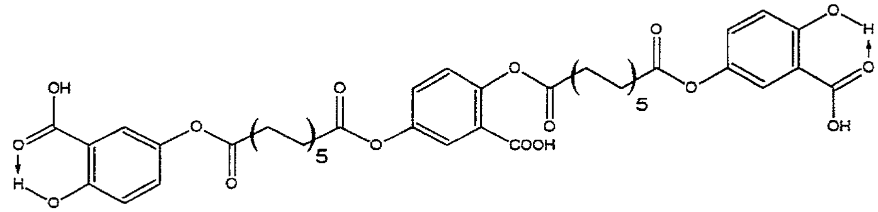
Figure 1. ^{1}H NMR (270 MHz, d_8-THF) spectra of oligomers, $\mathbf{G_nD_{n-1}}$ (top) and $\mathbf{MeG_nD_{n-1}}$ (bottom) in the aromatic region.

Figure 2. Infra-red absorbance spectra of $\mathbf{G_nD_{n-1}}$ (top) and $\mathbf{MeG_nD_{n-1}}$ (bottom) oligomers.

Figure 3. DAD HPLC of $\mathbf{G_3D_2}$ showing oligomeric components $\mathbf{g_2d_1}$, $\mathbf{g_3d_2}$, $\mathbf{g_4d_3}$ and $\mathbf{g_5d_4}$.

Figure 4. details the results of Variable temperature viscometric analysis of $\mathbf{G_nD_{n-1}}$ (top) and $\mathbf{MeG_nD_{n-1}}$ (bottom) oligomers.

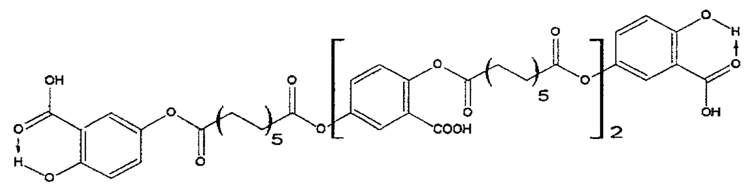
Example 1: Oligomers of the average structure G_3D_2:



A magnetically stirred melt of 2,5-dihydroxybenzoic acid (4.435 g, 29 mmol) **(G)**and dodecanedioyl dichloride (5.126 g, 19 mmol) **(D)**was heated from ambient temperature to 150 ^{0}C as rapidly as possible. Following 10 minutes stirring at this temperature, the viscous, transparent melt was poured from the vessel, solidifying to

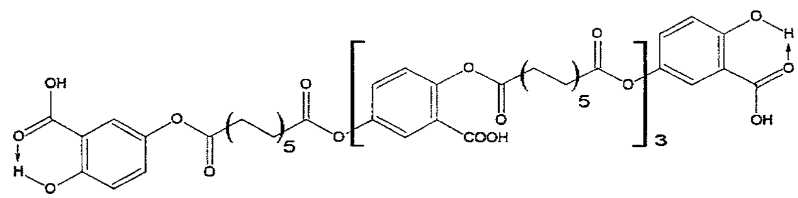
an opaque glass, and desiccated. IR / cm^{-1}: 1132, 1182, 1486, 1698, 1760, 2618, 2854, 2928, 3080. ^1H NMR (270 MHz; d_8-THF): δ11.04 (s (sharp), -OH); δ8.32 (s (broad), -COOH); 2,5-disubstituted **G**: δ7.72 (d, *J* 2.8, Ar-H); δ7.29 (dd, *J* 8.9, 2.8, Ar-H); δ7.08 (d, *J* 8.9, Ar-H); 5-substituted **G**: δ7.54 (d, *J* 2.8, Ar-H); δ7.18 (dd, *J* 8.9, 2.8, Ar-H); δ6.89 (d, *J* 8.9, Ar-H); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$). Electrospray MS -ve ion: 501.1 $\mathbf{g_2d_1}$ 849.2 $\mathbf{g_3d_2}$, 1197.3 $\mathbf{g_4d_3}$ (M-H$^+$).

Example 2: Oligomers of the average structure G_4D_3:



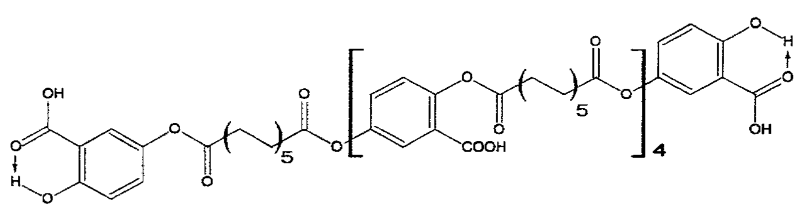
A magnetically stirred melt of 2,5-dihydroxybenzoic acid (4.115 g, 27 mmol) and dodecanedioyl dichloride (5.351 g, 20 mmol) was heated from ambient temperature to 150 ^{0}C as rapidly as possible. Following 10 minutes stirring at this temperature, the viscous, transparent melt was poured from the vessel, solidifying to an opaque glass, and desiccated. IR / cm^{-1}: 1132, 1182, 1486, 1698, 1760, 2618, 2854, 2928, 3080. ^1H NMR (270 MHz; d_8-THF): δ11.04 (s (sharp), -OH); δ8.32 (s (broad), -COOH); 2,5-disubstituted **G**: δ7.72 (d, *J* 2.8, Ar-H); δ7.29 (dd, *J* 8.9, 2.8, Ar-H); δ7.08 (d, *J* 8.9, Ar-H); 5-substituted **G**: δ7.54 (d, *J* 2.8, Ar-H); δ7.18 (dd, *J* 8.9, 2.8, Ar-H); δ6.89 (d, *J* 8.9, Ar-H); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$). Electrospray MS -ve ion: 501.1 $\mathbf{g_2d_1}$, 849.2 $\mathbf{g_3d_2}$, 1197.3 $\mathbf{g_4d_3}$, 1545.4 $\mathbf{g_5d_4}$, 1893.5 $\mathbf{g_6d_5}$ (M-H$^+$).

Example 3: Oligomers of the average structure G_5D_4:



A magnetically stirred melt of 2,5-dihydroxybenzoic acid (3.610 g, 23 mmol) **(G)**and dodecanedioyl dichloride (5.006 g, 19 mmol) **(D)**was heated from ambient temperature to 150 ^{0}C as rapidly as possible. Following 10 minutes stirring at this temperature, the viscous, transparent melt was poured from the vessel, solidifying to a semi-transparent glass, and desiccated. IR / cm^{-1}: 1132, 1182, 1486, 1698, 1760, 2618, 2854, 2928, 3080. ^{1}H NMR (270 MHz; d_8-THF): δ11.04 (s (sharp), -OH); δ8.32 (s (broad), -COOH); 2,5-disubstituted **G**: δ7.72 (d, *J* 2.8, Ar-H); δ7.29 (dd, *J* 8.9, 2.8, Ar-H); δ7.08 (d, *J* 8.9, Ar-H); 5-substituted **G**: δ7.54 (d, *J* 2.8, Ar-H); δ7.18 (dd, *J* 8.9, 2.8, Ar-H); δ6.89 (d, *J* 8.9, Ar-H); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$).

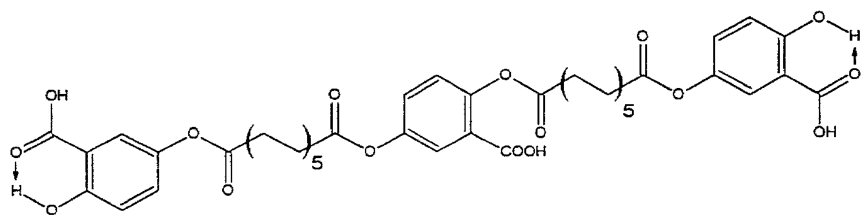
Example 4: Oligomers of the average structure G_6D_5:



A magnetically stirred melt of 2,5-dihydroxybenzoic acid (3.481 g, 23 mmol) **(G)**and dodecanedioyl dichloride (5.009 g, 19 mmol) **(D)** was heated from ambient temperature to 150 ^{0}C as rapidly as possible. Following 10 minutes stirring at this temperature, the viscous, transparent melt was poured from the vessel, solidifying to a semi-transparent glass, and desiccated. IR / cm^{-1}: 1132, 1182, 1486, 1698, 1760, 2618, 2854, 2928, 3080. ^{1}H NMR (270 MHz; d_8-

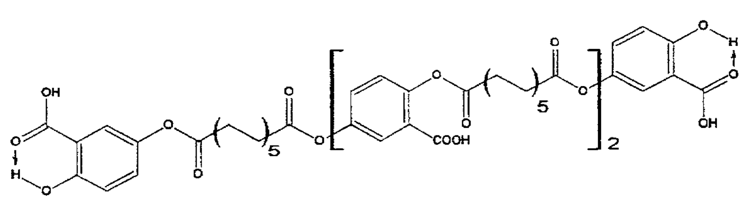
THF): δ11.04 (s (sharp), -OH); δ8.32 (s (broad), -COOH); 2,5-disubstituted **G**: δ7.72 (d, *J* 2.8, Ar-H); δ7.29 (dd, *J* 8.9, 2.8, Ar-H); δ7.08 (d, *J* 8.9, Ar-H); 5-substituted **G**: δ7.54 (d, *J* 2.8, Ar-H); δ7.18 (dd, *J* 8.9, 2.8, Ar-H); δ6.89 (d, *J* 8.9, Ar-H); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$).

Example 5: Oligomer of the structure g_3d_2:



The oligomer of average structure $\mathbf{G_3D_2}$ (example 1) was separated by preparative-scale LC into its constituent oligomeric components, resulting in the isolation of $\mathbf{g_3d_2}$. IR / cm^{-1}: 1132, 1182, 1486, 1698, 1760, 2618, 2854, 2928, 3080. ^1H NMR (270 MHz; d_8-THF): δ11.04 (s (sharp), -OH); δ8.32 (s (broad), -COOH); 2,5-disubstituted **G**: δ7.72 (d, *J* 2.8, Ar-H); δ7.29 (dd, *J* 8.9, 2.8, Ar-H); δ7.08 (d, *J* 8.9, Ar-H); 5-substituted **G**: δ7.54 (d, *J* 2.8, Ar-H); δ7.18 (dd, *J* 8.9, 2.8, Ar-H); δ6.89 (d, *J* 8.9, Ar-H); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$). Electrospray MS -ve ion: 849.2 ($M-H^+$).

Example 6: Oligomer of the structure g_4d_3:



The oligomer of average structure $\mathbf{G_3D_2}$ (example 1) was separated by preparative-scale LC into its constituent oligomeric components, resulting in the isolation of $\mathbf{g_4d_3}$. IR / cm^{-1}: 1132, 1182, 1486, 1698,

1760, 2618, 2854, 2928, 3080. ^{1}H NMR (270 MHz; d_8-THF): δ11.04 (s (sharp), -OH); δ8.32 (s (broad), -COOH); 2,5-disubstituted **G**: δ7.72 (d, *J* 2.8, Ar-H); δ7.29 (dd, *J* 8.9, 2.8, Ar-H); δ7.08 (d, *J* 8.9, Ar-H); 5-substituted **G**: δ7.54 (d, *J* 2.8, Ar-H); δ7.18 (dd, *J* 8.9, 2.8, Ar-H); δ6.89 (d, *J* 8.9, Ar-H); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, γδεCH_2). Electrospray MS -ve ion: 1197.3 ($M-H^+$).

Example 7: Oligomer of the average structure G_3D_3

A magnetically stirred melt of 2,5-dihydroxybenzoic acid (7.518 g, 49 mmol) and dodecanedioyl chloride (13.034 g, 49 mmol) was heated to 150 ^{0}C. Following 10 minutes of heating at this temperature, the transparent viscous melt was cooled to room temperature and desiccated.

Mechanical Properties

The mechanical properties of some of the supramolecular assemblies of the present invention are given below.

Aluminium studs were provided with a raised circular portion 5mm in diameter. A melt of the oligomers listed in Table 1 were coated onto the raised circular portions and the coated circular portions two studs were brought and held together under hand pressure until the melt had cooled and solidified. For comparative purposes a pair of aluminium studs were joined together with a conventional cyanoacrylate adhesive in the same manner as the supra molecular assemblies of the invention

Each stud was held in the jaws of a Nene MC 30000 tensile testing machine and testing was carried out a speed of 5mm min^{-1}.

Table 1

Example	Oligomer	Load to break / N	Breaking strength / MPa
	G_2D_1	50	1.8
1	G_3D_2	413	15.1
2	G_4D_3	222	8.1
3	G_5D_4	105	3.8
4	G_6D_5	202	7.4
	Cyanoacrylate	193	7.1

For physical comparison with examples 1-4, equivalent oligomers were prepared using methyl-2,5-dihydroxybenzoate (**MeG**) in place of 2,5-dihydroxybenzoic acid:

COMPARATIVE EXAMPLES

(i) - Oligomers of average structure MeG_3D_2

A magnetically stirred melt of methyl-2,5-dihydroxybenzoate (2.461 g, 15 mmol) and dodecanedioyl dichloride (2.607 g, 10 mmol) was heated from ambient temperature to 150 ^{0}C as rapidly as possible. Following 10 minutes stirring at this temperature, the viscous, transparent melt was poured from the vessel, solidifying to an opaque glass, and desiccated. IR / cm^{-1}: 1129, 1212, 1486, 1682, 1731, 1761, 2854, 2928. ^{1}H NMR (270 MHz; d_8-THF): δ10.60 (2H, s (sharp), -OH); 2,5-disubstituted **MeG**: δ7.69 (d, *J* 3.0, Ar-H); δ7.31 (dd, *J* 8.7, 2.8, Ar-H); δ7.11 (d, *J* 8.7, Ar-H); δ3.78 (s, CH_3); 5-substituted **MeG**: δ7.52 (d, *J* 3.0, Ar-H); δ7.21 (dd, *J* 8.7, 3.0, Ar-H); δ6.93 (d, *J* 8.7, Ar-H); δ3.91 (s, CH_3); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$).

(ii) - Oligomers of average structure MeG_4D_3

A magnetically stirred melt of methyl-2,5-dihydroxybenzoate (2.426 g, 14 mmol) and dodecanedioyl dichloride (2.892 g, 11 mmol) was heated from ambient temperature to 150 ^{0}C as rapidly as possible. Following 10 minutes stirring at this temperature, the viscous, transparent melt was poured from the vessel, solidifying to an

opaque glass, and desiccated. IR / cm^{-1}: 1129, 1212, 1486, 1682, 1731, 1761, 2854, 2928. ^1H NMR (270 MHz; d_8-THF): δ10.60 (2H, s (sharp), -OH); 2,5-disubstituted **MeG**: δ7.69 (d, *J* 3.0, Ar-H); δ7.31 (dd, *J* 8.7, 2.8, Ar-H); δ7.11 (d, *J* 8.7, Ar-H); δ3.78 (s, CH_3); 5-substituted **MeG**: δ7.52 (d, *J* 3.0, Ar-H); δ7.21 (dd, *J* 8.7, 3.0, Ar-H); δ6.93 (d, *J* 8.7, Ar-H); δ3.91 (s, CH_3); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$).

(iii) - Oligomers of average structure MeG_5D_4

A magnetically stirred melt of methyl-2,5-dihydroxybenzoate (3.934 g, 23 mmol) and dodecanedioyl dichloride (5.013 g, 19 mmol) was heated from ambient temperature to 150 ^{0}C as rapidly as possible. Following 10 minutes stirring at this temperature, the viscous, transparent melt was poured from the vessel, solidifying to a semi-transparent glass, and desiccated. IR / cm^{-1}: 1129, 1212, 1486, 1682, 1731, 1761, 2854, 2928. ^1H NMR (270 MHz; d_8-THF): δ10.60 (2H, s (sharp), -OH); 2,5-disubstituted **MeG**: δ7.69 (d, *J* 3.0, Ar-H); δ7.31 (dd, *J* 8.7, 2.8, Ar-H); δ7.11 (d, *J* 8.7, Ar-H); δ3.78 (s, CH_3); 5-substituted **MeG**: δ7.52 (d, *J* 3.0, Ar-H); δ7.21 (dd, *J* 8.7, 3.0, Ar-H); δ6.93 (d, *J* 8.7, Ar-H); δ3.91 (s, CH_3); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$).

(iv) - Oligomers of average structure MeG_6D_5

A magnetically stirred melt of methyl-2,5-dihydroxybenzoate (3.778 g, 23 mmol) and dodecanedioyl dichloride (5.016 g, 19 mmol) was heated from ambient temperature to 150 ^{0}C as rapidly as possible. Following 10 minutes stirring at this temperature, the viscous, transparent melt was poured from the vessel, solidifying to a semi-transparent glass, and desiccated. IR / cm^{-1}: 1129, 1212, 1486, 1682, 1731, 1761, 2854, 2928. ^1H NMR (270 MHz; d_8-THF): δ10.60 (2H, s (sharp), -OH); 2,5-disubstituted **MeG**: δ7.69 (d, *J* 3.0, Ar-H);

δ7.31 (dd, *J* 8.7, 2.8, Ar-H); δ7.11 (d, *J* 8.7, Ar-H); δ3.78 (s, CH_3); 5-substituted **MeG**: δ7.52 (d, *J* 3.0, Ar-H); δ7.21 (dd, *J* 8.7, 3.0, Ar-H); δ6.93 (d, *J* 8.7, Ar-H); δ3.91 (s, CH_3); **D** δ2.51 (t, *J* 7.2, αCH_2); δ1.69 (m, βCH_2); δ1.36 (m, $\gamma\delta\varepsilon CH_2$).

The MeG-oligomers so produced differed from the examples of the invention in that the potential for intermolecular acid hydrogen bonding had been removed.

Structural and oligomeric homology between the **G**-based and **MeG**-based oligomers was confirmed by ^1H NMR spectroscopy, as shown in Figure 1. The presence of acidic hydrogen bonding functionality in the **G**-based oligomers and the absence of such functionality in **MeG**-based oligomers manifested itself when the IR spectra of the two series were compiled and compared, as seen in Figure 2. The absorbance band-broadening observed in the carbonyl region (ca. 1700 cm^{-1}) for **G**-based oligomers is indicative of several hydrogen bonding environments, in comparison with relatively sharp absorbances in corresponding **MeG**-based oligomers.

The oligomeric distribution for examples of average structure was determined by liquid chromatography with a UV-vis diode array detector. The results shown in Figure 3 illustrate the distribution of oligomers in the Supramolecular Assembly described in Example 1. The proposed physical effect of multiple-site intermolecular hydrogen bonding interactions was confirmed by variable temperature viscometric study of **G**-based and **MeG**-based oligomers, as shown in Figure 4. The viscosities for **G**-based oligomers were consistently greater than those observed for **MeG**-based oligomers by *ca.* 40-fold. It can also be seen that, in general, viscosities increased, throughout the temperature range observed,

as the average oligomeric length increased. Viscosities increased with a greater rate towards solidification as the average oligomeric length increased. These observations are in accordance with an increasing number of intermolecular hydrogen bonding interactions and entanglements.

All $\mathbf{G_nD_{n-1}}$ oligomers formed fibres from the molten state that became brittle after several minutes at room temperature; $\mathbf{MeG_nD_{n-1}}$ oligomers were non-fibre-forming. All $\mathbf{G_nD_{n-1}}$ and $\mathbf{MeG_nD_{n-1}}$ oligomers cooled to semi-transparent glasses.

CLAIMS

1. A supramolecular assembly comprising a plurality of hydrogen bonded molecules, each molecule contains regularly spaced, multiple site hydrogen bonding groups and wherein at least a proportion of the molecules are bonded to other molecules at sites other than at terminal locations

2 An assembly as claimed in claim 1 wherein the hydrogen bonded molecules are pharmacologically acceptable

3. An assembly as claimed in claim 1 or claim 2 wherein the hydrogen bonding sites are separated by hydrophobic moieties

4. An assembly as claimed in any one of claims 1 to 3 wherein the hydrophobic moiety is derived from an alkyl diacid or functional derivative thereof

5. A compound that is capable of being hydrogen bonded to form a supramolecular assembly having the general formula **(I)**:

$$\mathbf{A\text{-}X\text{-}(N\text{-}X)_n\text{-}A} \qquad \mathbf{(I)}$$

where:

A may be the same or different and is a moiety containing at least one hydrogen bond donor and/or acceptor sites,

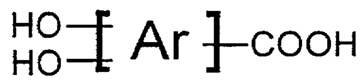
N may be the same or different and is a moiety containing at least one hydrogen bond donor and/or acceptor,

X may be the same or different and is a difunctional spacer linkage or unit

and **n** is an integer having a value of at least one.

6. A compound as claimed in claim 5 wherein the moieties **A** and **N**, contain hydroxyl or carboxyl groups

7. A compound as claimed in claim 5 or claim 6 wherein **A** is an aromatic moiety of the general formula **(II)**:



(II)

Where **Ar** is an unsubstituted or substituted aromatic nucleus.

8. A compound as claimed in any of claims to 7 wherein **Ar** is phenyl or benzyl

9. A compound as claimed in any of claims 5 to 8 wherein the compound of Formula (II) is 2,5- dihydroxybenzoic acid or 2,3-dihydroxybenzoic acid

10. A compound as claimed in any of claims 5 to 9 wherein **N** is a moiety containing at least three hydrogen bond acceptance or donation sites.

11. A compound as claimed in any of claims 5 to 10 wherein **X** is an alkyl diacid of the general formula:

$HOOC-(CH_2)_m-COOH$

Wherein m is an integer having a value of at least 2, or a functional derivative thereof

12. A compound as claimed in Claim 11 wherein **X** is derived

from dodecanedioic-, decanedioic-, octanedioic- or hexanedioic acids or an acid chloride thereof

13. An assembly comprising the aggregation of compounds of the general formula (I) as defined in claim 5

14. An artefact manufactured from an assembly as claimed in any one of claims 1 to 4 or from a compound as claimed in any one of claims 5 to 13

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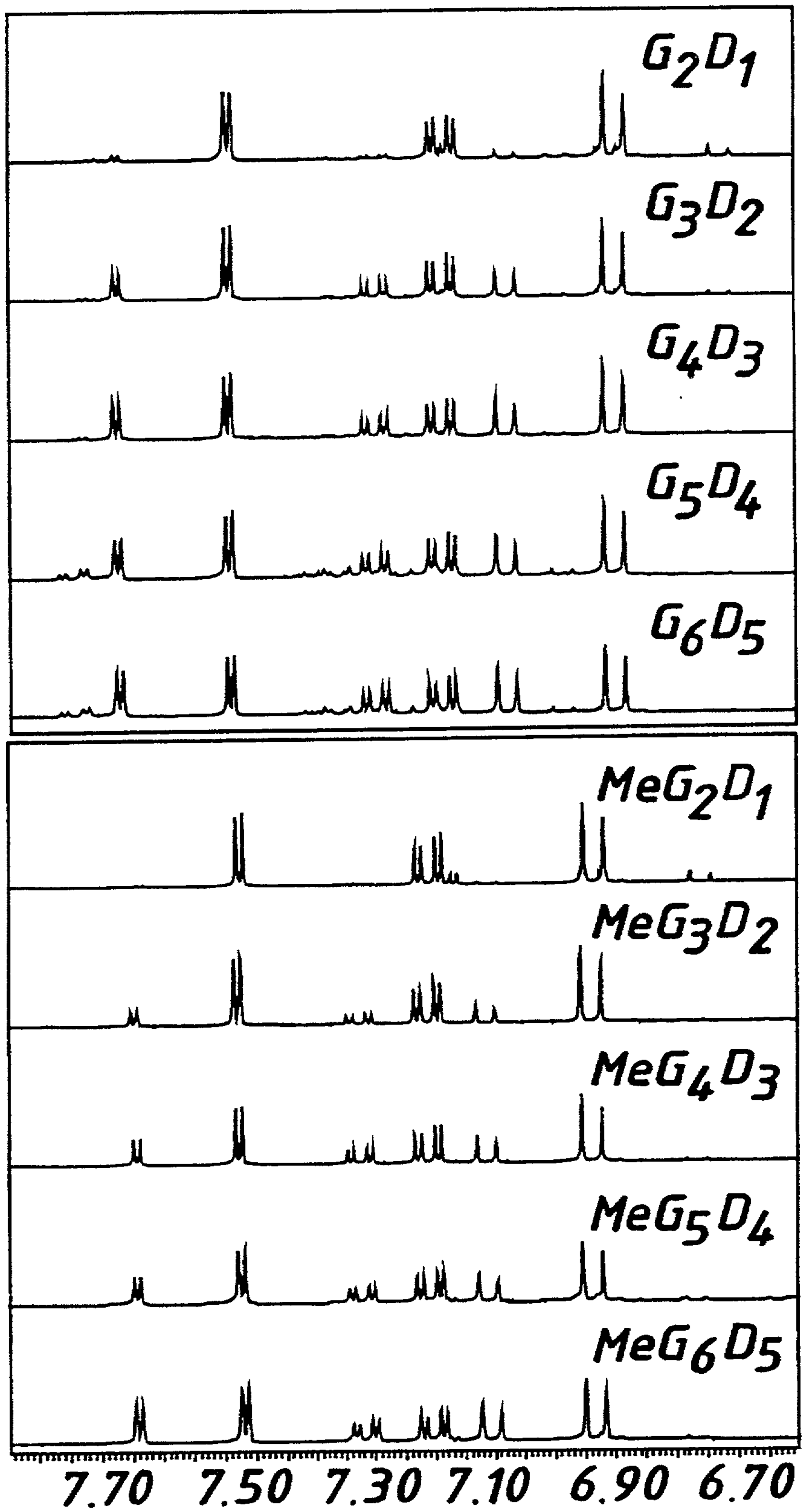
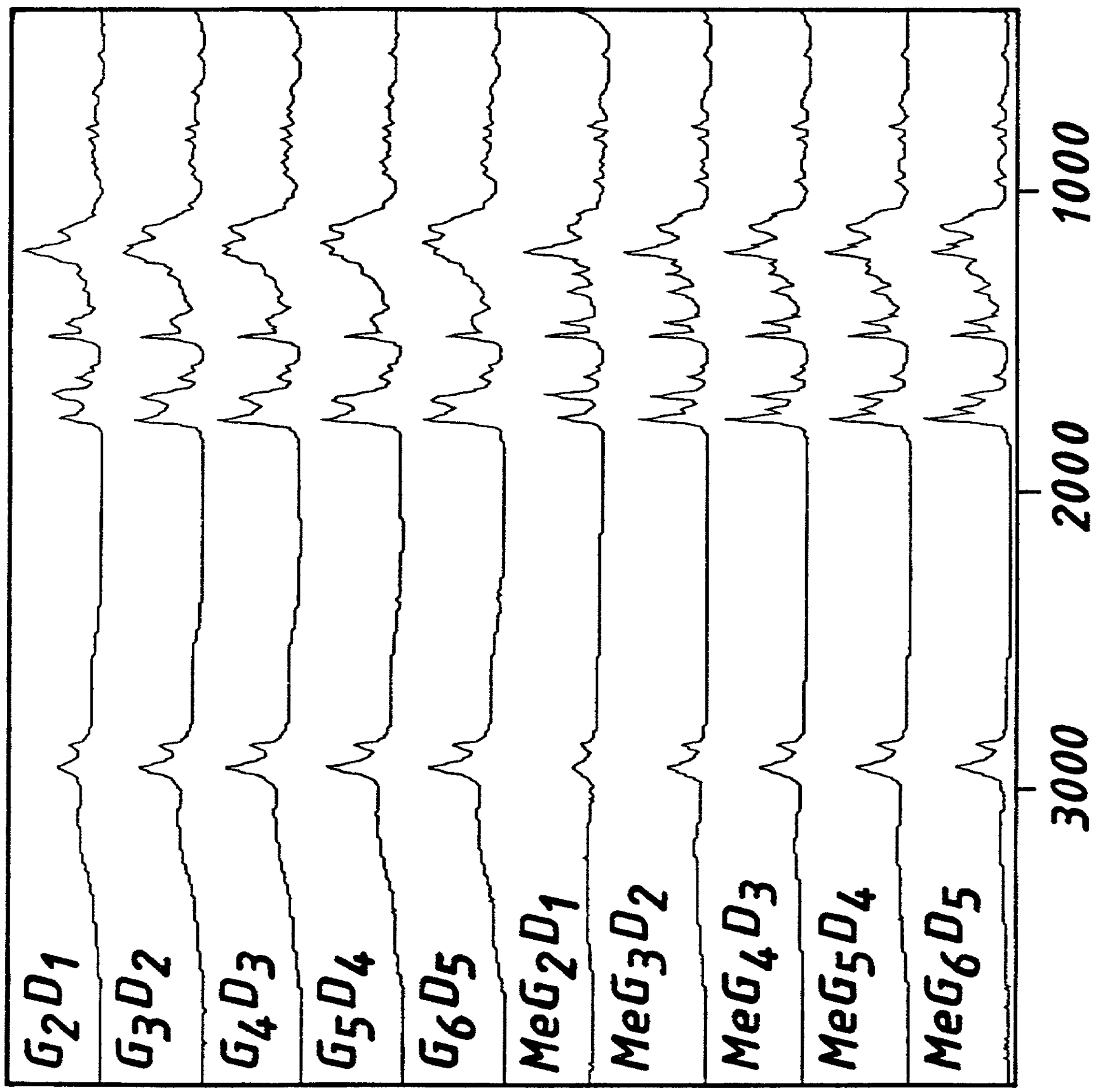
FIG. 1.



G2D1
G3D2
G4D3
G5D4
G6D5
MeG2D1
MeG3D2
MeG4D3
MeG5D4
MeG6D5
7.70
7.50
7.30
7.10
6.90
6.70
(ppm)



G_2D_1
G_3D_2
G_4D_3
G_5D_4
G_6D_5
MeG_2D_1
MeG_3D_2
MeG_4D_3
MeG_5D_4
MeG_6D_5
1000
2000
3000

FIG.2.

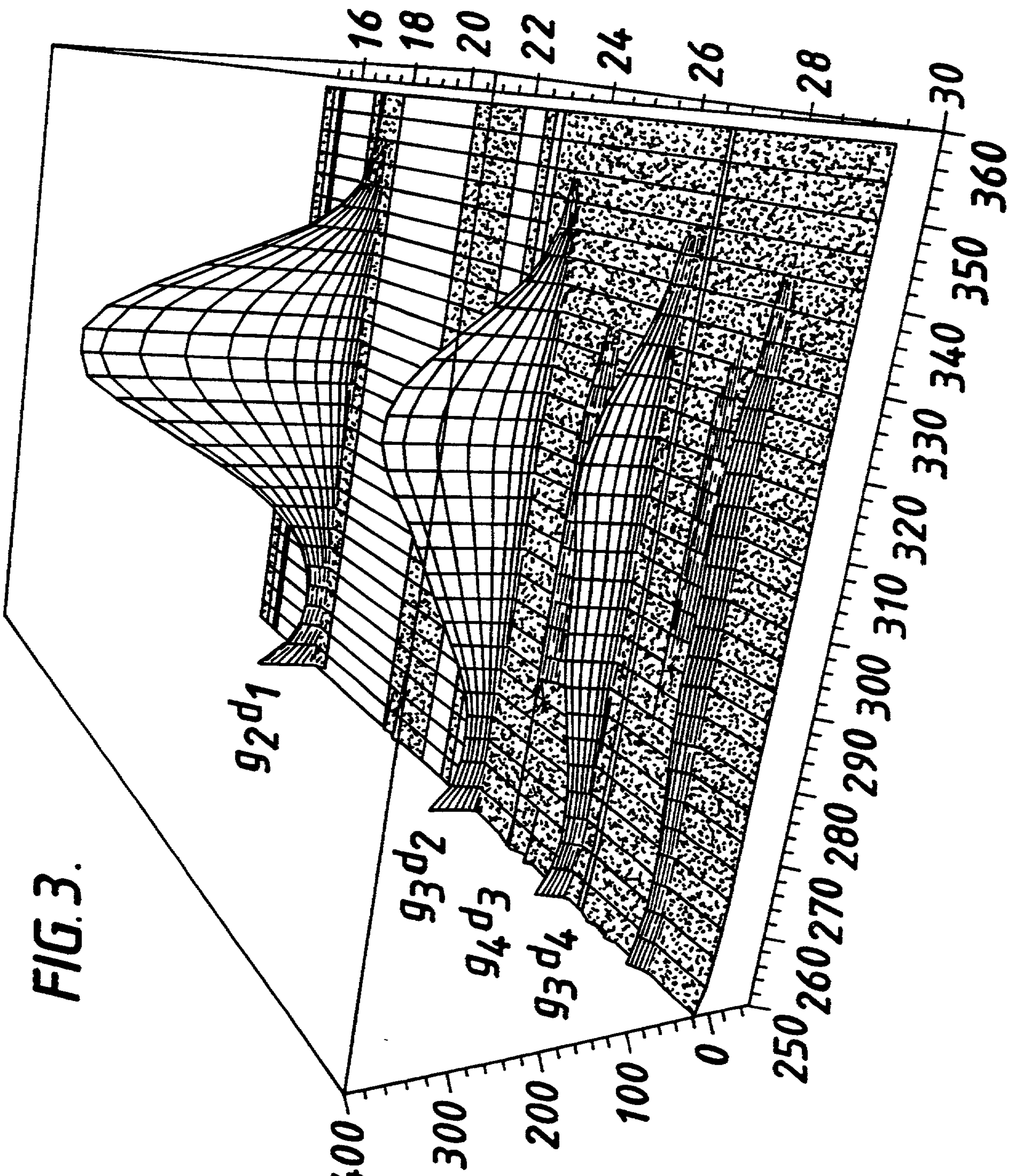

16
18
20
22
24
26
28
30
360
350
340
330
320
310
300
290
280
270
260
250
0
100
200
300
400
g_2d_1
g_3d_2
g_4d_3
g_3d_4

FIG. 3.

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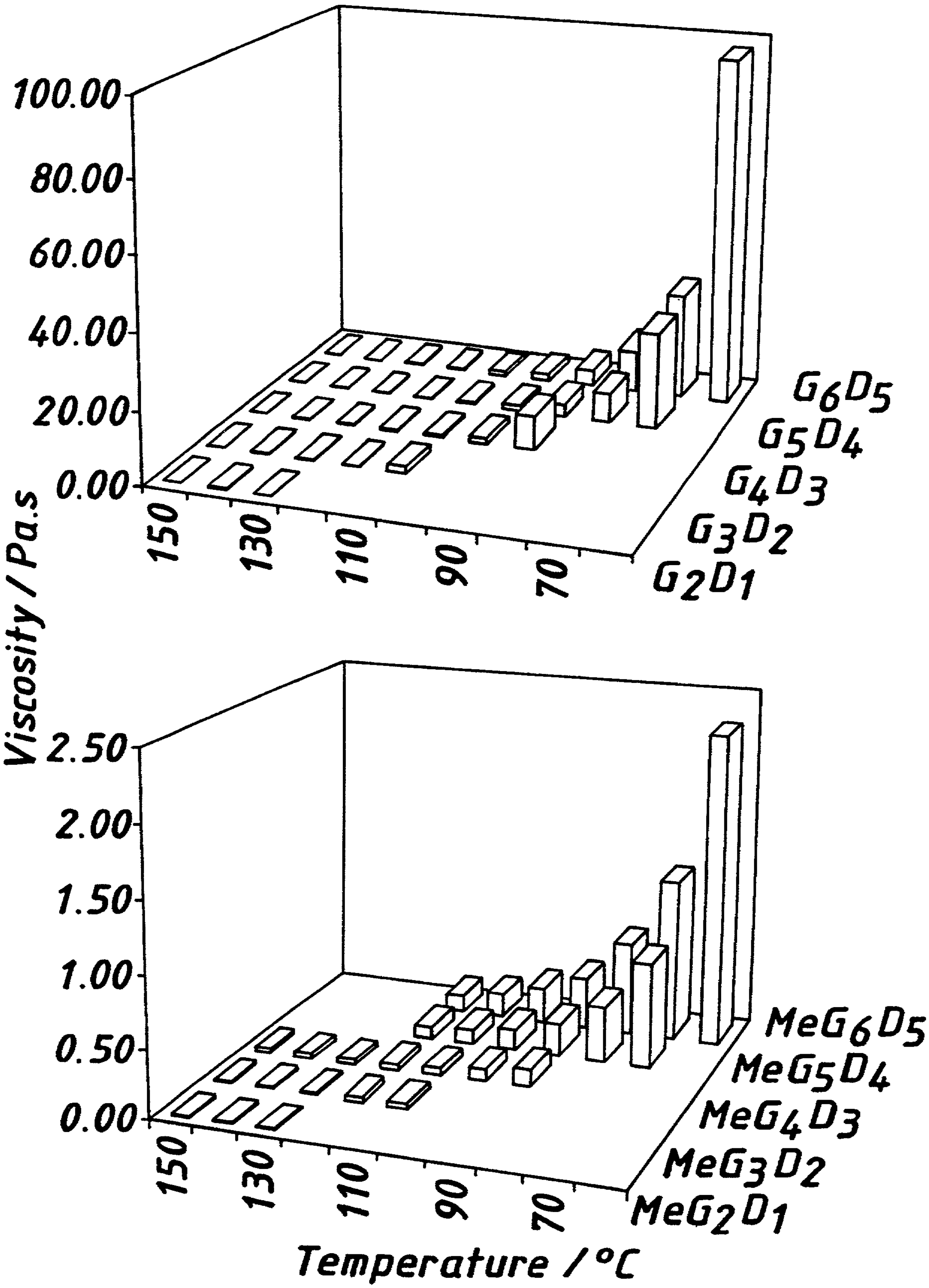
FIG. 4.


100.00
80.00
60.00
40.00
20.00
0.00
150
130
110
90
70
G6D5
G5D4
G4D3
G3D2
G2D1
Viscosity / Pa.s
2.50
2.00
1.50
1.00
0.50
0.00
150
130
110
90
70
MeG6D5
MeG5D4
MeG4D3
MeG3D2
MeG2D1
Temperature / °C

DECLARATION FOR USA PATENT APPLICATION

(including Design and National Stage PCT) Attorney's Docket ID: ____________

As a below named inventor, I hereby declare that:
My residence, post office address and citizenship are as stated below adjacent to my name. I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled Hydrogen Bonded Compounds
____________, the specification of which

____ is attached hereto. (or)
X was filed on 26.07.00, [ ] and was amended on ____________.

[ ] as U.S. Application No. ____________ or
[X] as International PCT Application No. GB00/02881

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, § 119 (a) - (d) or §365 (b) of any foreign application(s) for patent or inventor's certificate, or §365 (a) of any PCT International application which designated at least one country other than the United States of America, listed below and have also identified below, where priority is not claimed, any foreign application for patent or inventor's certificate, or any PCT International application, having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s) (____ ADDITIONAL APPLICATIONS IDENTIFIED ON ATTACHED SHEET):

Number	Country	Day/Month/Year Filed	Priority Not Claimed
9917461.7	GB	27 July 1999	

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s), or §365(c) of any PCT International application designating the U.S., listed below; and insofar as the subject matter of each claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations § 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application. (____ ADDITIONAL APPLICATIONS IDENTIFIED ON ATTACHED SHEET.)

Application Serial No.	Day/Month/Year Filed	Status -- patented, pending, abandoned

I hereby appoint the practioners of **LARSON & TAYLOR** associated with the Customer Number provided below to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith, and direct that all correspondence be addressed to that Customer Number.

CUSTOMER NUMBER: 00881

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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Full Post Office Address			
Residence - City, State/Country (if different from P.O. address)			
SIGN AND DATE HERE: Inventor's Signature:		Date:	

Full Name of Third Joint Inventor, if any		Citizenship	
Full Post Office Address			
Residence - City, State/Country (if different from P.O. address)			
SIGN AND DATE HERE: Inventor's Signature:		Date:	

Full Name of Fourth Joint Inventor, if any		Citizenship	
Full Post Office Address			
Residence - City, State/Country (if different from P.O. address)			
SIGN AND DATE HERE: Inventor's Signature:		Date:	

____ SEE ATTACHED SHEET FOR SIMILAR INFORMATION AND SIGNATURE FOR ADDITIONAL JOINT INVENTORS.
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